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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
MACFARLANE, STACEY NEE	
ART UNIT	PAPER NUMBER
1649	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/992,994	RASO, VICTOR	
	Examiner	Art Unit	
	STACEY MACFARLANE	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *85 and 86* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *85 and 86* is/are rejected.

7)☒ Claim(s) *85 and 86* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Claims 85 and 86 have been amended as requested in the amendment filed on September 17, 2009. Following the amendment, claims 85 and 86 are pending in the instant application, and are under examination in the instant office action.

2. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

Claim Objections

3. Claims 85 and 86 are objected to because of the following informalities: The brackets around the recitation "SEQ ID NO: 3" are taken as a typographical error and will be interpreted as parentheses. Double brackets within a claim are generally used to indicate a deletion where strike-through cannot easily be perceived. Appropriate correction is required.

4. Claims 85 and 86 are objected to because the preamble recites a method for forming an immune complex but the resultant step of the method is drawn to detection. Thus, the results of the method do not lead to the formation of an immune complex. Appropriate correction is required in order to better relate the preamble of the claim to the active steps of the method.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 85 stands as rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claim 85 is indefinite in its recitation of "physiological levels of human serum albumin".

8. On page 5 of Remarks filed September 17, 2009, Applicant traverses the rejection by stating the following:

> "One of skill in the art understands that 'physiological levels of albumin' constitute a physiological range. The Examiner has generously provided teachings demonstrating that one of ordinary skill in the art would be apprised of the scope of the claim containing the phrase 'physiological levels of albumin' by presenting references by those of skill in the art demonstrating the range of physiological levels of serum albumin. See, pending Office Action, page 4. In view of the Examiner's largess, the Applicant respectfully requests the withdrawal of the rejection".

While this has been considered it is not found persuasive to overcome the rejection for the following reasons. Examiner maintains that normal physiological levels of human serum albumin fall within the range of 35 to 55 mg/ml, known within the art. However, the "physiological levels" of the claim encompass levels that lie outside what is considered in the art to be normal levels and includes the physiological levels associated with hyperalbuminaemia, which occurs during exsiccosis, and hypoalbuminaemia, which occurs during Kwashiorkor disorder, for example. Thus, the

range of "physiological levels" is not finite, and one of ordinary skill in the art would not be reasonably apprised as to the scope of the invention.

9. As currently amended, Claim 86 is indefinite in its recitation of a method comprising detecting the immune complex in the presence of "about 60 mg/ml of human serum albumin". One of ordinary skill in the art would not be reasonably apprised as to whether a method that taught every other limitation within the claim but taught detection in the presence of, for example, 55 mg/ml or 65 mg/ml of albumin would fall within the metes and bounds of the invention. Thus, the scope of the claim is indefinite.

Claim Rejections - 35 USC § 101

10. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 85 and 86 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility.

Prior to focusing on the statutory requirements, it is important to determine precisely what the applicant has invented and how the claims relate to and define that invention. See *In re Abele*, 684 F.2d 902, 907, 214 USPQ 682, 687. The abstract of the application states the following:

> "The present invention provides an antibody which catalyzes hydrolysis of beta-amyloid at a predetermined amide linkage … Antibodies generated are characterized by the amide linkage which they hydrolyze. Specific antibodies provided include those which catalyze the hydrolysis at the amyloid linkages between residues 39 and 40, 40 and 41, and 41 and

> 42, of beta-amyloid. The present invention also provides a vectorized antibody which is characterized by the ability to cross the blood brain barrier and is also characterized by the ability to catalyze the hydrolysis of beta-amyloid at a predetermined amide linkage … The present invention also provides a method for sequestering free beta-amyloid in the bloodstream of an animal by intravenously administering antibodies specific for beta-amyloid to the animal in an amount sufficient to increase retention of beta-amyloid in the circulation. In addition, the present invention provides a method for sequestering free beta-amyloid in the bloodstream of an animal by immunizing an animal with an antigen comprised of an epitope which is present on beta-amyloid endogenous to the animal under conditions appropriate for the generation of antibodies which bind endogenous beta-amyloid. Therapeutic applications of these methods include treating patients diagnosed with, or at risk for Alzheimer's disease. Methods for reducing levels of beta-amyloid in the brain of an animal, by intravenously administering antibodies specific for endogenous beta-amyloid to the animal, or by immunizing the animal with an antigen comprised of an epitope which is present on endogenous beta-amyloid are also provided. In one embodiment, the antigen used to generate the antibodies is a transition state analog which mimics the transition state adopted by beta-amyloid during hydrolysis at a predetermined amide linkage. Similar methods which utilize or generate antibodies which catalyze the hydrolysis of beta-amyloid for reducing levels of circulating beta-amyloid in an animal, and also for preventing the formation of amyloid plaques in the brain of an animal, and also for disaggregating amyloid plaques present in the brain of an animal, are also provided. Also provided is a method for generating antibodies which catalyze hydrolysis of a protein or polypeptide by immunizing an animal with an antigen comprised of an epitope which has a statine analog which mimics the conformation of a predetermined hydrolysis transition state of the polypeptide. A similar method, which utilizes reduced peptide bond analogs to mimic the conformation of a hydrolysis transition state of a polypeptide, is also provided."

Thus the asserted utilities pertain to the specific methods comprising catalytic antibodies or antibodies which sequester and remove beta amyloid from the circulation. The claims, however, do not require a catalytic antibody, nor does the method of the invention require the sequestration of circulating beta amyloid. Rather, Claims 85 and 86 are drawn to a method for forming an immune complex comprising providing beta-amyloid in the presence of physiological levels (claim 85), or "up to 60 mg/ml" (claim 86), human serum albumin; forming an incubation mixture comprising these components and an antibody generated to the central region of SEQ ID NO: 3;

incubating the mixture under conditions appropriate for the binding of antibody to antigen and removing a sample from the incubation mixture to detect an immune complex of beta-amyloid and antibody in the presence of human serum albumin.

It should be noted that with the exception of the step requiring detection, the method fails to distinguish from naturally occurring immune complexes formed *in vivo* between autoantibodies and the central region beta-amyloid (See Figure 3, Gaskin et al., "Human Antibodies Reactive with β-Amyloid Protein in Alzheimer's Disease", *Journal of Experimental Medicine*, 177:1181-1186, 1993; and page 3880, lines 3-19 of Sohn et al., *Frontiers in Bioscience*, 14: 3879-3883, January 1, 2009).

Additionally, the instant application has provided no specific guidance as to how the method for formation of the immune complex is to be used. Rather, the assert utilities within the specification pertain to unclaimed embodiments drawn to "treating patients diagnosed with, or at risk for Alzheimer's disease" or "for reducing levels of circulating beta-amyloid in an animal, and also for preventing the formation of amyloid plaques in the brain". There is no specific utility for the formation of the immune complex of the claims. The statute under §101 requires a utility that provides a specific benefit in currently available form (*Brenner v. Manson*, 383, U.S. at 534-35, 148 USPQ at 695). *Brenner's* standard has been interpreted to mean that vague, general disclosures or arguments of "useful in research" or "useful as building blocks of value to the researcher" would not satisfy the criteria of §101. See *Kirk*, 376 F. 2d at 945 153 USPQ at 55 (interpreting Brenner). In the instant case, there is no specific usefulness asserted for the immune complex of the claims. The claims do not require a specific

catalytic antibody but are, rather, drawn to any antibody which binds the region defined as SEQ ID NO: 3. The specification states, "Specific antibodies provided include those which catalyze the hydrolysis at the amyloid linkages between residues 39 and 40, 40 and 41, and 41 and 42, of beta-amyloid". However, the antibody of the claims binds SEQ ID NO: 3, residues 9 through 25 of beta-amyloid (See Figure 3 of the Specification), which excludes this amyloid linkage region. Since there is no asserted utility for the immune complex of the invention, then its usefulness is merely one which is applicable to the formation of any immune complex, in general. Therefore, the claims lack specific utility.

Furthermore, assuming *arguendo* that the claimed method fulfilled the requirements of specific utility, the court *In re Fisher* (2005 WL 2139421 (CAFC Sept. 7, 2005) stated that § 101 requires a utility that is both specific and substantial. A substantial utility is defined as one having a real-world practical application, or has an asserted use that shows "that the claimed invention has a significant and presently available benefit to the public". Within the art, the detection of autoantibody immune complexes sometimes has practical applications for the diagnosis of autoimmune diseases, such as Lupus or Myasthenia Gravis. However, there is nothing within the instant specification that relates the methods, as claimed, to a utility of diagnosis. In fact, the word "diagnosis" or "diagnosing" are not found within the disclosure as originally filed. The only related reference pertains to unclaimed embodiments which "can be of therapeutic benefit to … a human who has a family history of Alzheimer's disease, or who is diagnosed with the disease" (paragraph [0037], for example),

implicating diagnosis occurs prior to embarking upon the methods of the disclosure. Furthermore, even within the current state of the art, beta amyloid autoantibodies are known to be detectable in both control and Alzheimer disease patients (Sohn et al., 2009, page 3880, last paragraph) and have no well-established diagnostic application. Thus, one of ordinary skill in the art would not easily recognize the practical application of the method for forming an immune complex and detecting said complex, as claimed. Since there is nothing within the instant specification that relates the methods to any real-world practical application, then the invention lacks substantial utility.

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 85 and 86 are also rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Additionally, to the extent that the claims 85 and 86 read upon the detection of an immune complex between beta amyloid and an antibody specific for beta amyloid, wherein said detection occurs in human serum, then the claims contains subject matter which was not described in the specification in such a way as to enable one skilled in

the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Even within the current state of the art, “a circulating serum antibody against A-beta … has not [been] identified yet” (page 3880, lines 6-8, Sohn et al., 2009 cited above). Additionally, in the art at the time of filing, it was known that "the presence of circulating β-AP may preclude the detection of circulating anti-β-amyloid antibodies and provides an explanation for our inability to detect these antibodies in the patients’ sera” (page 1185, first full paragraph of Gaskin et al., 1993, cited above). Therefore, without specific guidance as to how to overcome these obstacles, the specification does not provide enabling support such that one of ordinary skill in the art would be able to perform the method comprising detecting the immune complex in serum, with a reasonable expectation of success.

Conclusion

13. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STACEY MACFARLANE whose telephone number is (571)270-3057. The examiner can normally be reached on M-R 5:45 to 3:30, TELEWORK-Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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